REMARKS/ARGUMENTS

Claims 1, 6, 8-21, 25-43 and 45-61 are under examination in the application. Claims 4, 5, 7, 22-24, 44 and 62-80 have been cancelled. The Office Action mailed on February 22, 2008 includes the following rejections:

1. Claims 1, 6, 8-21, 25-43 and 45-61 are rejected under 35 U.S.C. § 103(a).
2. Claims 1, 6, 8-21, 25-43 and 45-61 are rejected under 35 U.S.C. § 103(a).
3. Claims 1, 6, 8-21, 25-43 and 45-61 are rejected under 35 U.S.C. § 112, first paragraph.

Claim Rejections – Claims 1, 5-22, 24-43 and 45-61 are rejected under 35 U.S.C. § 103(a)

The Office Action maintained the rejections of claims 1, 6, 8-21, 25-43 and 45-61 under 35 U.S.C. § 103(a) as being unpatentable over Devane, et al., U.S. Patent No. 6,228,398 (Devane), in view of Dang, et al., U.S. Patent No. 6,462,094 (Dang) and the Office Action also rejected claims 1, 6, 8-21, 25-43 and 45-61 under 35 U.S.C. § 103(a) as being unpatentable over Devane in view of Dang and Davis et al., U.S. Patent Application No. 2003/0049318 ("Davis"). Applicants submit that the references, either alone or in any combination, fail to meet the standard of rejection under 35 U.S.C. § 103.

> In order to establish a prima facie case of obviousness, three criteria must be met: (1) there must be some suggestion or motivation in the prior art to modify the reference or to combine reference teachings as proposed, (2) there must be a reasonable expectation of success, and (3) the prior art or combined references must teach or suggest **all** the claim limitations. (emphasis added) MPEP § 2143; *In re Vacek*, 947 F.2d 488 (Fed. Cir.1991). "The prior art must suggest the desirability of the claimed invention." MPEP § 2143.01.

Applicants submit that the references, either alone or in any combination, fail to meet the standard of rejection under 35 U.S.C. § 103 because (1) it fails to teach every element of the present invention and (2) the proposed modification or combination of references would change the principle of operation of the prior art invention being modified thus eliminate the expectation of success and motivations to combine.

First, Applicants submit that the references, either alone or in any combination, fail to teach every element of the present invention. Looking closely at the release profile in Devane, the product

taught therein for immediate release only provides 50% of the first active in about 2 hours. Devane's extended, pulsate release only achieves 50% release in about 6 hours. In contrast, the present invention provides release of over 80% of the first active within about 60 minutes. Therefore, Devane does not achieve the release profiles taught by the present Application. Devane simply fails to achieve the claimed release profiles, and does not teach every element of the present Application.

Furthermore, Devane is not enabling as to any modifications of the release profile or how to modify those release profiles. In fact, Devane discloses in the claims (e.g., claim 19) the release profiles of 50 to 100% within four hours as also shown in Devane Figure 1 and 25 to 55% release between four to eight hours. Devane's Table 4 discloses that between 76 and 87% release is only obtained at 10 hours. Also looking at Tables 3 and 4, a maximum of 50.5% release was obtained after one hour.

Dang teaches a conventional tablet prepared by well-known conventional tabletting techniques that includes phenylephrine tannate and guaifenesin. Dang does not teach a first active available for immediate release and a second active for extended release that are released during the required timeframes and does not provide the claimed release profile. The addition of Dang fails to teach any manner to achieve the claim release. Devane fails to add the missing preparation of the release profiles as claimed. The combination of Devane and Dang does not teach each and every element of the present Application.

Davis teaches a drug product having two portions both of which contain guaifenesin. Davis teaches a compressed bi-layer tablet with an immediate release formulation of guaifenesin and a delayed release matrix formulation of guaifenesin, Davis does not teach an enveloped formulation that combines a first active on a carrier and a second active on a carrier. The delayed release matrix formulation of Davis is simply a media that when exposed to low pH forms a gel from which the guaifenesin diffuses. Using the teachings in Davis the skilled artisan would not be able to achieve the present invention.

The combination of Devane and Dang and Davis fails to teach each and every element of the present Application. Specifically, a first active available for immediate release, having over 80% of the first active released within 60 minutes; and a second active for extended release

selected from a decongestant, an antihistamine, an antitussive and mixtures thereof, wherein the first active is disposed on a carriers and the second active is disposed on a bead, wherein the second active comprises three or more layers of the second active agent and an extended release coating and wherein over 80% of the second active is released between 90 minutes and 6 hours. The combination fails to establish a *prima facie* case of obviousness.

Devane fails to teach the claimed profile. The addition of the immediate release and extended release of Dang and the addition of Davis do not cure these deficiencies. The combination still fails to teach a first active available for immediate release, having over 80% of the first active released within 60 minutes; and a second active for extended release selected from a decongestant, an antihistamine, an antitussive and mixtures thereof, wherein the first active is disposed on a carriers and the second active is disposed on a bead, wherein the second active comprises three or more layers of the second active agent and an extended release coating and wherein over 80% of the second active is released between 90 minutes and 6 hours. The combination of Devane, Dang and Davis simply fails to teach every element of the present Application.

Second, Applicants assert that there are no expectation of success nor motivations to combine because the proposed combination of the references would change the principle of operation of the prior art invention being modified and are not sufficient to render the claims *prima facie* obvious.

> See, MPEP Section 2143.01(V) states that "[i]f proposed modification would render the prior art invention being modified unsatisfactory for its **intended purpose**, then there is no suggestion or motivation to make the proposed modification." Likewise, MPEP Section 2143.01 (VI) states "[i]f the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious." (emphasis added)

There is no likelihood of success or motivation to combine because the combination would yield the combination unsatisfactory for the desired function. Devane's release is **substantially delayed**, and Devane prefers the second active to be almost completely delayed for at least two hours i.e., a pulsed manner (Col. 10 Line 52-64). This means that there are little to no drug available in-between the two pulses.

> cleared from the patient's system. In a preferred embodiment, release of the active ingredient from the second component of the composition in operation is substantially, if not completely, delayed for a period of at least about two hours after administration of the composition.

Devane's objective is further illustrated in the following paragraph, wherein Devane's delayed release is useful for drugs susceptible to patient tolerance (col. 6 Line 16-20). It is not desirable for Devane to have a "sustained release" where drugs are consistently present.

> present invention. Particularly usefull in the practice of the invention include active ingredients whose pharmacological and/or therapeutic effects benefit from having a wash-out period between plasma concentration peaks, such as those active ingredients susceptible to the development of patient tolerance. Example active ingredients include but are not

Thus, the combination of references would result in a pharmaceutical composition that releases two active ingredients in a **pulsed, bimodal** way where the active ingredients are not consistently present in a subject due to the need of preventing drug tolerance.

The present invention provides a **sustained-release** of the active ingredients. It is undesirable to have a pulsated release profile because the present invention provides a prolong decongestion and expectorant relief to a subject, as evident by the release profile, paragraphs [0005], [0016] and throughout the Specification. A skilled artisan would recognize that the combination of references ***teaches away*** from the claimed invention when it is reviewed as a whole. As such, the combination of references would change the intended purpose of the present invention. Accordingly, the combination of references fails to establish a *prima facie* obviousness.

For the reasons stated above, Applicants respectfully submit that claims 1, 6, 8-21, 25-43 and 45-61 are not obvious over Devane, Dang and Davis, therefore, allowable under 35 U.S.C. § 103(a). Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 103.

Claim Rejections--Claims 1, 6, 8-21, 25-43 and 45-61 are rejected under 35 U.S.C. § 112, first paragraph

The Office Action rejected claims 1, 6, 8-21, 25-43 and 45-61 under 35 U.S.C. § 112, first paragraph base on the assertion that the claims contains subject matters that was not described in the written description sufficiently to convey a skilled artisan that the inventors were in possession of

the present invention. Applicants respectfully disagrees such assertion.

The pharmaceutical compositions and release profiles are described in detailed description of the application, specific examples and guidance of sufficient, relevant, identifying characteristics are provided throughout the specification. Applicants understand that the specification does not read limitations into the claims; however, Applicants also understand that the claims must be viewed in light of the specification and given its broadest reasonable interpretation consistent with the written description.

Possession may be shown in many ways. For example, possession may be shown by describing an actual reduction to practice of the claimed invention. Possession may also be shown by a clear depiction of the invention in detailed drawings or in structural chemical formulas which permit a person skilled in the art to clearly recognize that applicant had possession of the claimed invention. An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. See, e.g., *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) (the written description "inquiry is a factual one and must be assessed on a case-by-case basis"). As such, the present specification as filed provides sufficient, relevant, identifying characteristics to show a person skilled in the art that the inventor had possession of the claimed invention.

The Office Action asserted the following as the bases of the rejection:

> In the above examples, there is no description of what the composition is enveloped in, what excipients allow for the claimed release profile of the first active agent, what the carrier is composed of, what the beads are composed of, or what extended release excipients allow for the

Applicant disagrees with the Office Action's assertion that there is no description of what the composition is enveloped. Paragraph [0025] of the Specification provides details of what "enveloped" means in the present Application. In addition, since claims are part of the Specification, claim 1 specifically point out the composition is an enveloped pharmaceutical and paragraph [0025] further defines examples of enveloped pharmaceuticals.

> [0025] A number of definitions are provided herein to facilitate an understanding of the present invention. As used herein, the term "enveloped pharmaceutical" means a capsule, a suppository, a gel cap, a softgel, a lozenge, a sachet or even a fast dissolving wafer. As used herein the term "carrier" is used to describe a substance, whether biodegradable or not, that is physiologically acceptable for human or animal use and may be pharmacologically active or inactive.

Furthermore, the skilled artisan would readily know and understand the term enveloped. The Examiner is reminded that not everything necessary to practice the invention need be disclosed, in fact, what is well known is best omitted. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). It is not necessary to specify every term known to the skilled artisan.

The Office Action also asserted the following:

> second active agents. Accordingly, other than the specific formulations described in the examples (pages 23-25), Applicants have not described the enveloping materials, excipients, carriers, or extended release coatings that would result in the claimed first and second active agent release profiles.

Applicants respectfully disagree with this assertion. As illustrated in the various examples shown from paragraphs [0080] to [0099], specific formulation shown would enable a skilled artisan to perform and reproduce the present claims and release profiles, thus putting the invention in public's possession. Other data such as the table shown in paragraph [0098] further demonstrates examples that may be used to achieve the claimed invention. An assertion cannot be made by ignoring such examples. Further, the Office Action stated:

> Aside from the very limited examples provided in the specification, Applicants provide no direction as to (a) what excipients and extended release coatings out of all possible excipients and release coatings that exist in the art would have been reasonably expected to result in the claimed release profiles and (b) which of those excipients and extended release coatings actually *do* result in the claimed release profiles without having to execute hit or miss testing practices in order to make such a determination.

Applicants respectfully disagree with the assertion that the examples are "very limited" in the present Application and remind the examiner that examples are not a requirement. However, the present specification provides more than adequate support in the numerous examples disclosed herein. For example, the specification provides in paragraph [0081] capsule shells and processes, paragraph [0082] discloses four different levels of sustained release coating amounts were added. Paragraph [0085] discloses the dissolution rate of the phenylephrine that is accelerated when combined with Gauifenesin DC. Paragraph [0086] discloses the stability of capsules. In addition numerous examples are disclosed in the specification including in paragraph [0088], Formula I, a batch of immediate release first active, e.g., guaifenesin for use with the enveloped formulation, in paragraph [0089], Formula II, a batch of immediate release guaifenesin for use with the enveloped formulation, in paragraph [0090], Formula III, paragraph [0091], Formula IV, and paragraph [0092], Formula V. In addition, numerous formulations were also disclosed in the specification, e.g., paragraph [0094] disclosed a formulation for immediate release of a first active and extended release of a second active in an enveloped formulation, in a gelcap; Paragraph [0095] disclosed a formulation for immediate release of a first active and extended release of a second active in an enveloped formulation, in a suppository; Paragraph [0096] disclosed an effervescent tablet for immediate release of a first active and extended release of a second active in an enveloped formulation, in an effervescent tablet; and Paragraph [0097] disclosed an immediate release of a first active and extended release of a second active in an enveloped formulation one may add the following ingredients, in a caplet. In addition, paragraph [0098] summarizes some of the Examples in the Specification and lists various first and second actives in the table.

Similar to the arguments made above, one cannot ignore the examples shown in the

Specification as filed. The Specification does provide sufficient information such as curing temperature, tablet compact strength and formulas that enable a skilled artisan to achieve the claimed invention. Contrary to the Office Action's assertion, these examples are not limited and a skilled artisan would be able to reproduce the claimed invention using at least the examples shown in the Specification.

With respect to the "step-plus-function" named in the Office Action:

> Further, though Applicants have limited the claimed compositions to those that have particular release profiles of active agents, it remains that Applicants have not appropriately defined the metes and bounds of the claimed compositions, even when limited by function (step-plus-function form). As taught in the MPEP at § 2163, step-plus-function claims are not

Applicants submit that all the claims are related to a pharmaceutical composition; these are not method claims that achieve particular functions. Applicants have clearly defined the "Metes and Bounds" of the claimed composition. Specifically the present invention claims an enveloped pharmaceutical composition having a first active available for immediate release, wherein over 80% of the first active is released within 60 minutes; and a second active for extended release selected from the group consisting of a decongestant, an antihistamine, an antitussive and mixtures thereof, wherein the first active is disposed on a carriers and the second active is disposed on a bead, wherein the second active comprises three or more layers of the second active agent and an extended release coating and wherein over 80% of the second active is released between 90 minutes and 6 hours. Accordingly, Applicants respectfully request withdrawn of the §112 rejections.

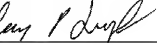
Conclusion

Claims 1, 6, 8-21, 25-43 and 45-61 are pending in the above-identified Application. Withdrawal of the objections and rejections and an early Notice of Allowance are earnestly requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Dated: May 22, 2008

Respectfully submitted,



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